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Pharmaceutical Benefit-Risk Perception and Older Age: A Pilot Study

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Abstract

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Keywords: older age, benefit-risk perception, pharmaceuticals, affect

(1.) Background

Understanding how patients perceive the benefits and risks of medicines is a "pre-requisite" for effective pharmaceutical benefit-risk communication.[1] Risk perception knowledge can be used to correct patient misconceptions, strengthen accurate beliefs and add missing information that is 'material' to decision-making.[2-4] Interventions informed by perception research can close the gap between what patients know and what they need to know.[5] Communicators such as regulatory authorities, including the European Medicines Agency and the US Food and Drug Administration, and patient advocacy groups can more effectively achieve their communication goals.[6-10] Utilising risk perception knowledge ultimately contributes to ensuring medicines are used safely and effectively.

Benefit-risk perception research has evolved significantly,[1,5,6,11] however; only a small corpus of work has investigated the role of older age as a central focus of study.[12] One issue is that few psychological judgement and decision-making studies on ageing have been conducted in applied pharmaceutical contexts.[12] Since the US National Research Council published two influential reports[13,14] in the 2000s, psychological research on ageing has advanced substantially (*see* Hess *et al*.[15]). However, studies have focused more on basic neurobiological and behavioural mechanisms than understanding "the specific contexts in which older adults function" (p6).[16] This has limited scholars to *suggesting* ways that findings from non-risk contexts are *likely* to be important for benefit-risk communication.[17-19] Bruine de Bruin[19], for instance, explained how findings on age-related changes in cognitive deliberation, experience-based knowledge, emotions and motivation *might* inform interventions such as decision aids, training, delegation and 'nudge-based' approaches. While these suggestions are constructive, pharmaceutical benefit-risk communication tools would be better informed by more contextually-relevant risk perception knowledge.

A second issue is that few risk perception studies have investigated the role of age as a central focus of study. Early risk perception studies were frequently limited to younger student populations. More recently, thousands of studies have collected risk perception data and either not reported age-related results, or presented age as a confounder of a stronger relationship with another variable such as gender, risk beliefs or trust.[20] Rather than focusing on (older) age, researchers have been more interested in the characteristics of hazards (dread, uncertainty, controllability), or other characteristics of perceivers (gender, race, socio-economic status).[21-26]

There is now considerable evidence that older age must be investigated more carefully, critically and extensively.[15-20] Not least because, in the pharmaceutical context, most older adults use prescription and over-the-counter medicines, older adults consume the highest percentage of medicines by age group, and, to compound these factors, virtually every country in the world is experiencing growth in the number and proportion of older persons.[27-29] In addition, more responsibility has shifted to adults of all ages with trends towards empowering patients through shared decision-making, informed choice and the right to challenge physicians.[30-32]

This pilot study explored the role of older age in pharmaceutical benefit-risk perception. The primary goal was to generate experimental evidence to inform future pharmaceutical benefit-risk perception research on age-related effects across the adult life span. The two main research objectives were to (1) compare older versus younger adults' pharmaceutical benefit-risk perceptions and identify clear age-related differences; and (2) explore qualitatively how older

adults make quantitative judgements about the benefits and risks of various medicines, medical procedures, and tests.

(2.) Methods

A questionnaire, modelled on nationally representative surveys conducted in Sweden, Canada, and the US by Paul Slovic and colleagues,[1,33,34] was developed in 2017. A key difference between the present study and those by Slovic *et al*. was the addition of various open-ended questions. This generated extensive qualitative data on *why* respondents gave their benefit-risk judgements. The initial questionnaire was piloted face-to-face with a convenience sample of five respondents aged over 55 years old from London (UK) or Boulder, Colorado (USA). This informed three main changes: a slideshow visual aid was added to assist respondents in understanding survey questions; the questionnaire was shortened substantially; and minor wording changes were made. The study was approved by King College London's Research Ethics Office (MR/17/18-278).

(2.1) Sample

A total of 80 respondents were recruited from Boulder County, Colorado (USA) and Dublin (Ireland) (hereafter, Boulder and Dublin). Respondents were recruited through convenience sampling using online adverts and by approaching members of the public in cafés, public libraries and quiet hotel lobbies, as well snowball sampling through the interviewers' private networks. Demographic data was collected for both samples on age, sex, education and employment (Table 1). Data was also collected on two general indicators of health behaviour: whether respondents (1) currently have a doctor and (2) smoke cigarettes.

Table 1: Demographic and health information for older and younger samples

	Older Sample	**Younger Sample**

Dates		Nov. 1st – 10th, 2017	Feb 1st – 14th, 2018
Sample size		40	40
Age Range		58 to 93	31 to 50
Mean Age		72	39
Male		44%	45%
Education (%)	*Some schooling complete/ No high school diploma*	23%	0%
	High School Graduate or Equivalent	18%	30%
	Bachelor's Degree	21%	50%
	Master's Degree	36%	20%
	Professional/ Doctorate Degree	3%	0%
Employment (%)	*Working Full-Time*	13%	45%
	Working Part-Time	23%	25%
	Retired	64%	3%
	Full Time Homemaker	0%	5%
	Unemployed (looking for work)	0%	8%
	Student	0%	10%
	Other	0%	5%
Do you currently have a doctor? (%)	*Yes*	97%	60%
Do you currently smoke? (%)	*Yes*	0%	35%

Older Group. The older sample had 40 respondents from Boulder (N=20) and Dublin (N=20). They had a mean age of 72, their ages ranged from 58 to 93, and 44% were male. The large majority (87%) were either retired (64%) or working part-time (23%) and only 13% were working full-time. 60% had a bachelor's degree or higher, while 23% had only some schooling/ no high school diploma. None smoked and 97% had a doctor.

Younger Group. The younger sample had 40 respondents from Boulder (N=20) and Dublin (N=20). They had a mean age of 39, their ages ranged from 31 to 50 and 45% were male. The large majority (80%) were either working full-time (45%), working part-time (25%), or students (10%). 70% had a bachelor's degree or higher, and all younger group respondents had graduated from high school or equivalent. 35% smoked and 60% had a doctor.

(2.2) Survey administration

Surveys were conducted in November 2017 (older sample) and February 2018 (younger sample). They were administered face-to-face by the lead author and 3 trained research assistants. Face-to-face interviewing generated in-depth qualitative data. 78/80 survey interviews were audio recorded and transcribed[1].

Part 1: Words associated to prescription medicines.

Respondents were asked to indicate the first thought or association that comes to mind when reading the words "Prescription Medicines". The stimulus was shown on a laptop and not read aloud. The question was repeated twice more[2]. This continued associations technique is "a sensitive indicator of the imagery and meaning associated with people's mental representations for a wide variety of concepts" (p82).[1]

Part 2: General questions on medicines and other technologies

Perceptions of how risks have changed over time. Respondents were asked whether they believe there is more risk, less risk or about the same risk today than there was 20 years ago from sixteen separate items (Table 2). Similar questions about how risks have changed over time were included in past surveys examining risks to life generally (e.g. Harris[35]) and for a variety of specific hazards (e.g. Slovic *et al*.[1,21]). The sixteen items are hazards with a variety of characteristics (dread potential, familiarity, control, voluntariness) and are managed in differing policy contexts (healthcare, energy, pharmaceuticals, health and safety). Some items were selected from past studies, others were unique to this study.

[1] Two respondents consented to be interviewed but did not consent to being audio recorded.
[2] When piloting the present survey face-to-face it quickly became clear that respondents struggled to make more than 3 associations.

Table 2: Sixteen hazard items

Air travel	Heart disease
Adults getting Alzheimer's disease	Hurricanes
Cancer	Adults getting HIV/AIDS
Climate change	Nuclear power
Diabetes	Pesticides
Driving a car	Adults taking prescription medicines
Doctors making prescribing errors	Train travel
Flooding	Chemicals

Performance of key actors. Respondents were asked to rate the performance of doctors, pharmacists, pharmaceutical regulatory agencies, pharmaceutical companies, and patients in making sure that prescription medicines are safe and effective. The ordering of each actor was randomised between respondents.

Experiences with and perceptions of side effects. Respondents were asked about their personal experiences with prescription medicine side effects. This included (1) how often they believe that medicines work as intended for patients, (2) how often they believe patients experience unwanted side effects, and (3) whether they have (knowingly) had a mild, moderate or severe side effect over the past five years. 8 further questions indicated what respondents perceive to be the causes of side effects including patients being unusually sensitive to medicines, patient not following instructions, and doctors prescribing the wrong dosage.

Part 3: Psychometric benefit and risk questions

Over the past 50 years, different approaches to measuring perceived benefit and perceived risk have evolved. In psychometric studies, respondents are asked to make quantitative judgements about the risks of various hazards and technologies. They provide a well-established and reliable method for measuring respondents' perceptions of benefit and risk quantitively. The

advantages and limitations of the psychometric paradigm have been discussed at length elsewhere.[36-39]

In the present study, numeric scaling methods were used. Respondents were asked to rate the risks and benefits of 27 medical and non-medical technologies and hazards on a scale of 1 to 7 (Box 1). Two questions were asked on benefits and risks of 17 medical technologies (i.e. medical treatments), and two further and almost identical questions on 10 non-medical technologies. The items were 14 prescription and over-the-counter medicines, 2 medical procedures, 2 medical tests, and 10 non-medical technologies (Table 3). Including questions that independently measure specific dimensions of risk perception – such as actual probability of experiencing harm, the severity of the consequences of that result, or affective components[40] – were intentionally excluded. Instead, by asking *general* risk perception questions, the authors could explore how respondents construed the 'risks' and 'benefits' themselves, as well as the different ways that older adults justify quantitative benefit-risk judgements.

Box 1: Psychometric risk and benefit questions

Risks of medical technologies (to those exposed). To what extent would you say that adults who are taking or undergoing this medical treatment are at risk[3] of experiencing personal harm from it? (1 = they are not at risk; 7 = they are very much at risk)
Benefits of medical technologies. In general, how beneficial do you consider this treatment to be? (1 = not at all beneficial; 7 = very beneficial)
Risks of non-medical technologies (to those exposed). To what extent would you say that adults who are exposed to the following are at risk[2] of experiencing personal harm from it? (1 = they are not at risk; 7 = they are very much at risk)
Benefits of non-medical technologies. In general, how beneficial do you consider the following items to be for those exposed to it? (1 = not at all beneficial; 7 = very beneficial)

After rating each technology from 1 to 7, respondents were asked why they gave their answer. The closed questions (quantitative measures) provided a *platform* for investigating the reasons behind respondents' benefit and risk perceptions (qualitative measures). Asking follow-up

[3] 'Risk' was intentionally not defined. Respondents were left to interpret what 'risk' meant for each technology.

questions for a total of 54 questions (27 items x 2 questions each), would have made the questionnaire too long leading to survey fatigue. Therefore, trained interviewers asked follow-up questions when it seemed appropriate to them.

Table 3: Medical and non-medical items surveyed

Medicines	Medical Procedures & Tests	Non-Medical Technologies
Medicine to treat depression	Heart surgery	Cell phones
Medicines to slow the progression of Alzheimer's disease	Medical x-rays	Nuclear power plants
Medicines to treat erectile dysfunction	Prostate screening tests	Pesticides
Antibiotics	Acupuncture	Cigarette smoking
Sleeping pills		High-fat foods
Herbal medicines		Genetically modified food
Cancer chemotherapy		Automobiles
Insulin		Alcoholic beverages
Medicines for cholesterol (e.g. statins)		Coffee
Vitamin pills		Air travel
Blood pressure medicines		
MMR vaccine		
Flu vaccine		
Allergy medicines		

(3.) Results

(3.1) Associations to Prescription Medicines

Respondents gave a total of 187 spontaneous associations to the term 'Prescription Medicines'. Although 3 associations were requested, many struggled to give more than 2 resulting in a mean average of 2.3 per respondent. Qualitative content analyses revealed 12 broad categories of associations (Table 4). The three most frequently associated images were of health care professionals (e.g. prescribing doctors or pharmacists) (15% of all associations), the benefits of medicines (e.g. medicines are helpful, beneficial or good) (11%), and types of disease or illness (11%). Other frequent images were of dependency, abuse, and over-prescribing (10%), names of specific drugs (9%), and side effects in general (7%).

Almost a quarter (24%) of all older group associations were to the benefits of medicines, compared to only 7% in the younger group. Concerns about expense were much higher in the older (10%) versus younger (2%) group. Only 5% of all older group associations were to images of dependency, abuse and over-prescribing. In contrast, this category was the second most common association in the younger group (15%) after general images of healthcare professionals (16%) and before types of disease and illness (11%).

Table 4: Spontaneous imagery associated to "Prescription Medicines"

	Older (%)	Younger (%)	All (%)
Helpful/Beneficial/Good	24	7	11
HCPs (e.g. "My Doctor")	14	16	15
Types of Disease and Illness	12	11	11
Expensive	10	2	6
Names of Specific Drugs	9	9	9
Side Effects	8	7	7
Own and Family Prescription Medicines	6	3	5
Dependency/Abuse/Over-Prescribing	5	15	10
Annoying/Want to Avoid if Possible	4	5	5
Industry Profits	2	4	3
General Safety	1	5	3
Other (e.g. Packaging)	7	15	14
No. of Responses	**93 (count)**	**94 (count)**	**187 (count)**

(3.2) Perceptions of How Risks have Changed Over Time

Respondents were asked whether they believe there is more risk, less risk or about the same risk today than there was 20 years ago from 16 items (Table 5). For 11/15 items over 50% of all respondents indicated greater perceived risk. The largest proportion of respondents believing there is 'more' risk was for climate change (94%), diabetes (78%), flooding (76%) and adults taking prescription medicines (74%). This was followed by hurricanes (71%), cancer (69%), chemicals (69%), adults getting Alzheimer's disease (65%), heart disease (65%), pesticides (63%), driving a car (53%), and nuclear power (50%). Fewer than half of respondents indicated greater perceived risk from doctors making prescribing errors (48%), adults getting HIV (35%), air travel (34%), and train travel (19%). A large percentage of

respondents indicated that they believe there is *less* risk today than 20 years ago for adults getting HIV (53%), air travel (50%), and train travel (46%). Fewer than 30% of all respondents indicated less risk for all 13 other items.

Older versus younger respondents were more likely to indicate higher perceived risk than 20 years ago for 14 out of 16 items. Over 20% more older respondents indicated greater perceived risk from chemicals (+23% older respondents indicating 'more' risk), flooding (+23%), and hurricanes (+23%). This was followed by adults getting HIV (+20%), doctors making prescribing errors (+20%), and train travel (+18%). Heart disease (-13% older respondents indicating 'more' risk) and cancer (-5%) were the only two items that fewer respondents from the older versus younger group perceived as riskier than 20 years ago.

Table 5: Percentage of all respondents (N=80) for the question: 'Do you think there is more, less, or about the same risk today than 20 years ago for the following items?'

	More	Less	About the Same
Climate Change	94	3	4
Diabetes	78	11	11
Flooding	76	6	18
Adults Taking Prescription Medicines	74	13	14
Hurricanes	71	4	25
Cancer	69	11	19
Chemicals	69	16	15
Adults Getting Alzheimer's Disease	65	8	26
Heart Disease	65	11	24
Pesticides	63	24	14
Driving a Car	53	29	19
Nuclear Power	50	23	28
Doctors Making Prescription Errors	48	21	30
Adults Getting HIV	35	53	10
Air Travel	34	50	16
Train Travel	19	46	35

(3.3) Ensuring Medicines are Safe and Effective

Respondents were asked to rate the job of five separate actors in making sure that prescription medicines are safe and effective (Table 6). Three quarters (75%) rated pharmacists as either

excellent (29%) or good (45%) in ensuring that medicines are safe and effective. Lower ratings were given to doctors (55% excellent or good), pharmaceutical companies (45%) and regulatory agencies (43%). At the bottom of the list, fewer than a third (28%) of respondents rated patients (taking Rx) as either excellent (4%) or good (24%) in making sure they are safe and effective; two-thirds (69%) rated patients as either doing a fair (35%) or poor (34%) job.

Older versus younger group respondents were much more likely to rate prescribing doctors as excellent or good in making sure that prescription medicines are safe and effective (73% versus 38%; +35% difference). Older versus younger respondents were also marginally more likely to rate all other actors are excellent or good by +10% for all four actors.

Table 6: Table showing the percentage (%) of older and younger group respondents that rated five actors as either excellent or good in making sure that prescription medicines are safe and effective.

	Older (%)	Younger (%)	All (%)
Pharmacists	80	70	75
Prescribing Doctors	73	38	55
Pharma Companies	50	40	45
Regulatory Agencies	48	38	43
Patients	33	23	28

(3.4) Effectiveness and Side Effects

Respondents were asked three related questions on the effectiveness and side effects of prescription medicines. First, the very large majority of all respondents believe that prescription medicines work at least often for patients (88% always, very often, often) (Table 7). All older group respondents (100%) indicated that prescription medicines are effective very often (43%) or often (58%). While most younger group respondents also indicated that prescription medicines are effective at least often (78% always, very often, often), slightly fewer than a quarter said that only occasionally work (23%). No respondents indicated that prescription medicines are rarely or never effective.

Second, the results show that 61% of respondents perceive that patients experience unwanted effects or side effects from prescription medicines at least often (Table 7). A concomitant proportion perceive that side effects occur only occasionally (31%) or rarely (8%). Little variation was found between older versus younger groups perception of unwanted effects of side effects occur . No respondents believed that unwanted effects or side effects occur never.

Table 7: Respondents perceptions of effectiveness and side effects. Effectiveness: "How often do you believe that prescription medicines work as intended for patients?" Side Effects: "How often do you believe that patients experience unwanted effects or side effects from prescription medicines?"

	Effectiveness			**Side Effects**		
	Older (%)	Younger (%)	All (%)	Older (%)	Younger (%)	All (%)
Always	0	3	1	3	10	6
Very Often	43	20	31	20	18	19
Often	58	55	56	43	30	36
Occasionally	0	23	11	30	33	31
Rarely or Never	0	0	0	5	10	8

Third, 60% of respondents said they have had a side effect from taking a prescription medicine over the past five years with 24% of all respondents indicating they have had a severe side effect, 22% indicating a moderate side effect and 14% indicting only mild side effects. A greater number of older versus younger respondents indicated they have experienced side effects over the past five years (+14% older respondents indicating 'yes').

Respondents were asked how often they think side effects from prescription medicines are caused by eight different explanations (Figure 1). The three most frequently perceived causes of side effects all related to patients. A large number of respondents perceived that patients not following instructions (58%), patients having insufficient information (49%) and patients being unusually sensitive to the prescription medicine (44%) are always, very often, or often a cause of side effects. This was followed by the patient's health plan restricting access to safer medicine (38% always, very often, or often a cause), a lack of government regulation (24%)

and the doctor prescribing the wrong dosage (16%). Few respondents indicated that the cause of a side effect is due to hospitals or pharmacists making mistakes (11% and 9%, respectively, rating always, very often, or often)

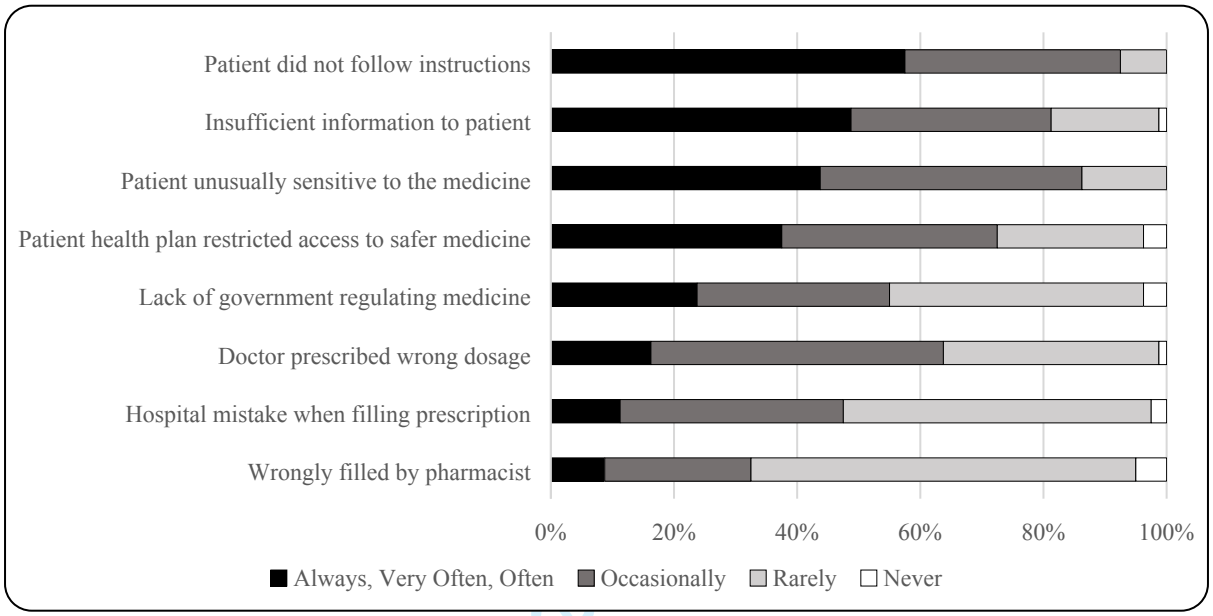

Figure 1: Bar chart showing how often all respondents (N=80) think side effects are caused by various explanations.

For both older and younger respondents, patients not following instructions, having insufficient information and being unusually sensitive to medicines were the three most frequently perceived causes of a side effect. The largest number of respondents (58%) in both the older and younger groups perceived patient not following instructions as the always, very often, or often the cause of a side effect. However, older versus younger respondents were more likely to perceive that hospital (+8% always, very often, often) and pharmacist (8%) mistakes as well as patient health plans restricting access to safer medicines (5%) are the cause of side effects. Older versus younger respondents were also less likely to perceive four other factors as being the cause of side effects: government regulation (-23% always, very often, or often), doctors prescribing the wrong dosage (-13%), patients being unusually sensitive to the medicine (-8%) and patients having insufficient information (-3%).

(3.7) Perceptions of Benefit and Risk

The geometric mean was calculated for respondents' risk ratings for all 27 medical and non-medical technologies (Figure 2). On the scale of 7 (they are very much at risk) to 1 (they are not at risk), the mean rating of perceived risk ranged from 6.35 (cigarette smoking) to 1.51 (acupuncture) (Figure X). The five technologies with the highest perceived risk were cigarette smoking, pesticides, nuclear power plants, high fat foods and alcoholic beverages. Four other technologies had a perceived risk of over 4.0: cancer chemotherapy, sleeping pills, heart surgery and automobiles. Acupuncture, prostate screening tests, vitamin pills, and coffee were perceived as having the lowest risk of experiencing personal harm from the technology.

The geometric mean was calculated for respondents' benefit ratings for all 27 medical and non-medical technologies (Figure 2). On the scale of 7 (very beneficial) to 1 (not at all beneficial), the mean rating of perceived benefit ranged from 6.00 (insulin) to 1.16 (cigarette smoking). The five technologies with the highest perceived benefit were insulin, medical X-rays, heart surgery, prostate screening tests and air travel. A further 10 technologies received a mean benefit rating of over 4.0. Cigarette smoking, high-fat foods, pesticides, genetically modified food (GMF), alcoholic beverages and nuclear power plants were perceived as having the lowest benefits with all six technologies receiving a mean rating of less than 3.0.

Differences between older versus younger respondents' risk and benefit perceptions were calculated by subtracting younger respondents mean risk and benefit ratings from older respondents mean risk and benefit ratings, respectively. For 21/27 technologies surveyed, older respondents had lower perceived risk than younger group respondents. Medicines to treat depression (-1.36 mean risk difference), genetically modified food (-1.13), and sleeping pills

(-1.01) topped the list of technologies that older respondents perceived as having less risk, which was closely followed by cancer chemotherapy (-0.91) and medicines to treat Alzheimer's Disease (-0.88). At the other end of the list, herbal medicines (0.87), cigarette smoking (0.51) and vitamin pills (0.23) were perceived as riskier by older respondents. Older versus younger respondents perceived less benefit for 16 out of 27 technologies. Herbal medicines (-1.54 mean benefit difference), medicines to treat Alzheimer's disease (-1.40), allergy medicines (-1.40) and prostate screening tests topped the list of technologies that older versus younger respondents perceived as having less benefit. This was followed by vitamin pills (-1.01), coffee (0.79) and heart surgery (-0.68). At the other end of the list, genetically modified food (0.96), pesticides (0.73) and cell phones (0.44) were perceived as more beneficial by older versus younger respondents.

The mean risk and mean benefit ratings were plotted onto a factor space (Figure 3). The plot quickly shows that all of the items clustered into one of four quadrants. Most medical technologies (11 out of 18) were perceived as high in benefit and low in risk (top-left quadrant). Cell phones and air travel were also perceived as high in benefit and low in risk. Heart surgery, automobiles, and cancer chemotherapy were perceived as high in benefit but also high in risk (top-right quadrant). Vitamin pills, coffee, herbal medicines and medicines for treating Alzheimer's Disease clustered together as technologies with low benefit and low risk (bottom left quadrant). Sleeping pills was the only medical technology that was perceived as being low in benefit and high in risk (bottom right quadrant). In contrast six non-medical technologies clustered into the low benefit and high-risk quadrant.

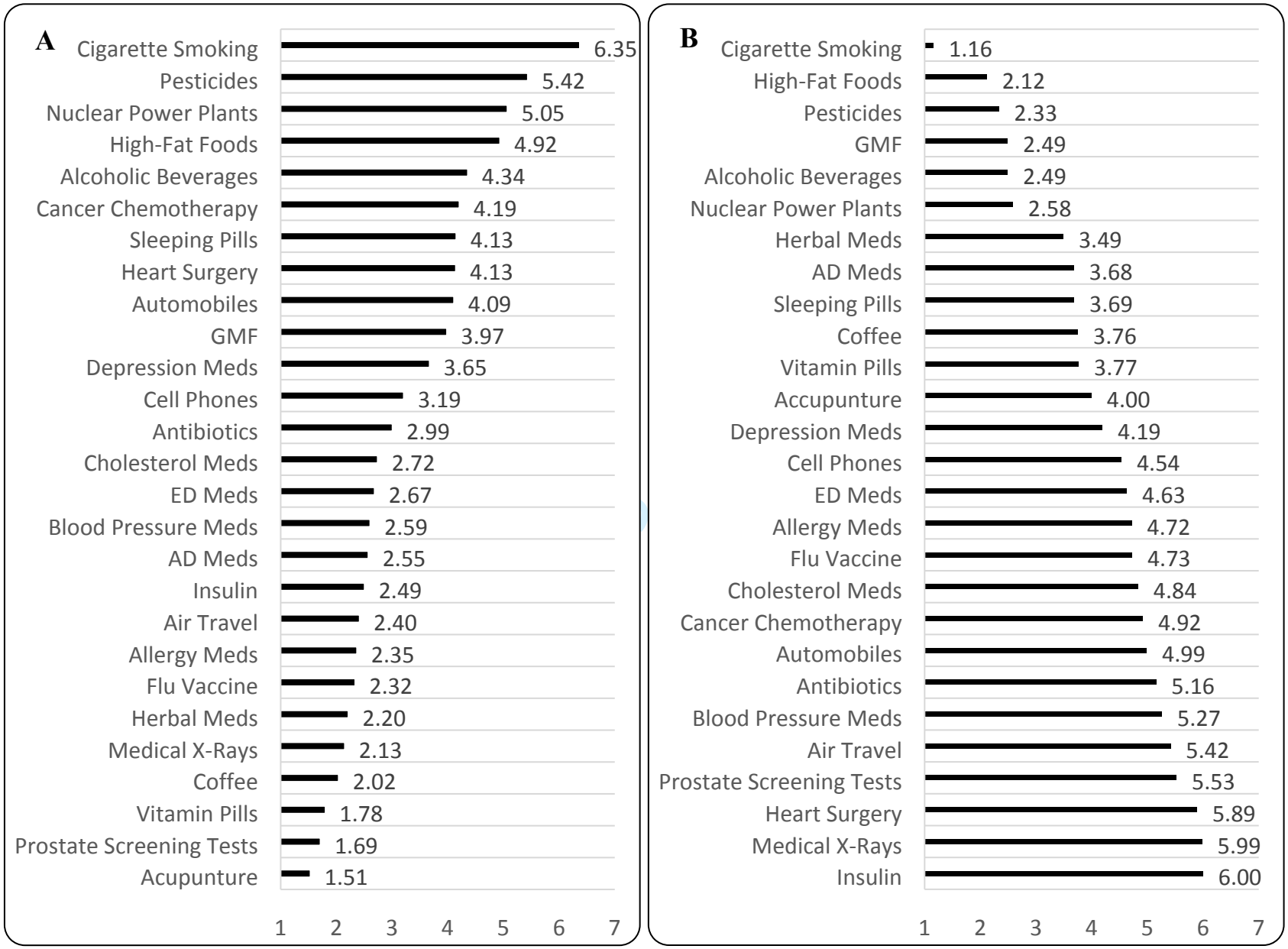

Figure 2:
(A) Mean Risk
(B) Mean Benefit
GMF: Genetically Modified Food
ED: Erectile Dysfunction
AD: Alzheimer's Disease

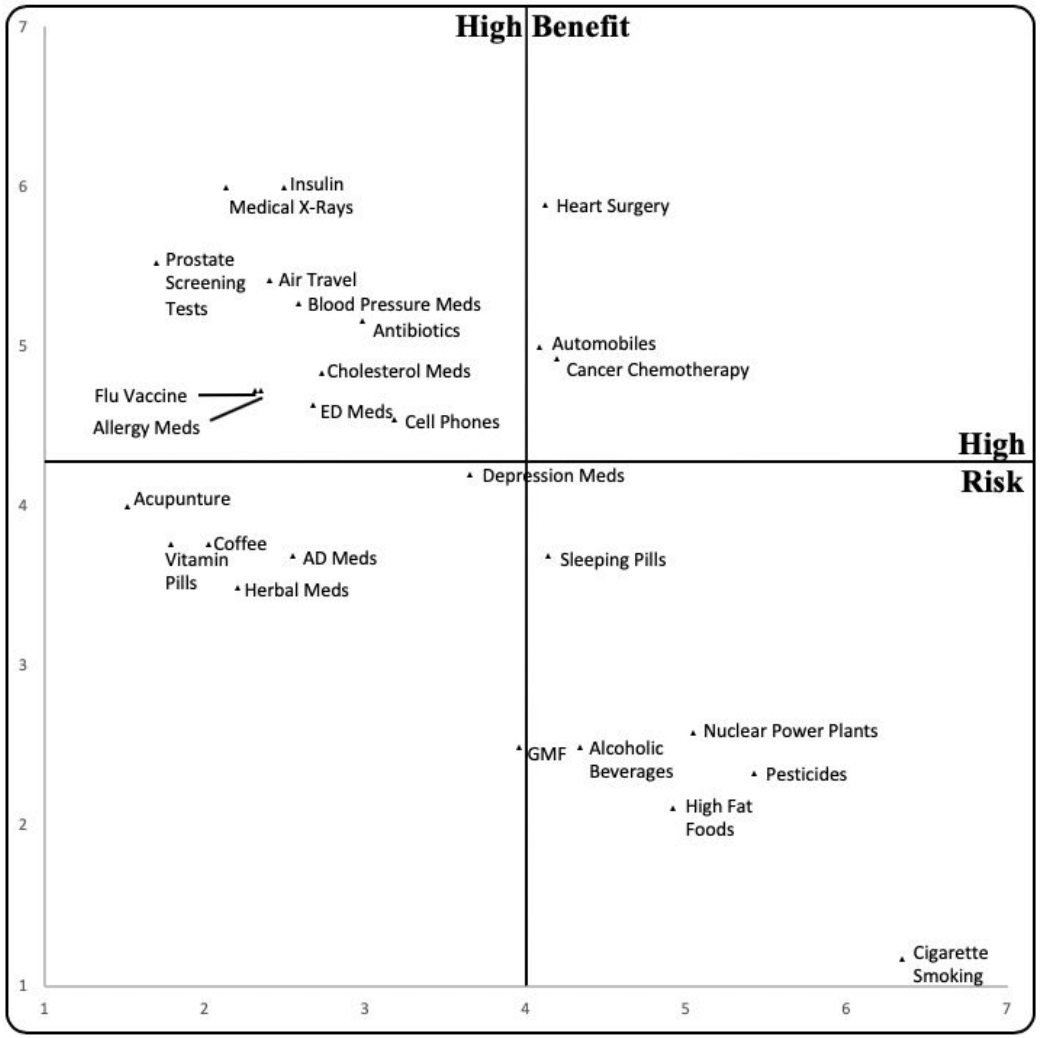

Figure 3: Plot of Benefit and Risk Means. GMF: Genetically Modified Food ED: Erectile Dysfunction AD: Alzheimer's Disease [High resolution image submitted separately].

(3.8) Justifications for Risk and Benefit Ratings

Older respondents were asked 'Why?' they gave their risk and benefit ratings for some but not all pharmaceutical items. A total of 276 open-ended responses were recorded and transcribed with an average of 8/34 open-ended follow-up questions per older group respondent. The authors coded and categorised responses using a qualitative content analysis.[41] The analysis revealed two main ways that respondents justified their risk and benefit ratings for pharmaceutical items: (1) describing risks and benefits, and (2) conveying experiences and feelings associated with each item.

Describing risks and benefits. The first main way that respondents justified their ratings was by simply describing the 'risks' and 'benefits' that they associated with different items (Table 8).

Table 8: Older respondents' (N=40) most common risk and benefit associations for all pharmaceutical items.

Item	Risks	Benefits
Medicines to treat depression	Suicide; over-dose; incorrect use	Benefits vary between patients; Patients need appropriate medicines
Medicines to treat Alzheimer's Disease	Low knowledge of any risks	Low knowledge of any benefits
Medicines to treat erectile dysfunction	Most unaware of any risks; Prolonged erections	Very effective for those who need them
Antibiotics	Antimicrobial resistance and over-use	Antimicrobial resistance reduces benefits
Sleeping pills	Over-dose; Dependency	Can really help patients fall asleep
Herbal medicines	Not harmful; Lack of regulation	Unconvinced about any benefits; False claims
Cancer chemotherapy	Risky treatment; Only hope for some people	Lifesaving for some; Many regret chemotherapy
Insulin	Few risks except with inappropriate use	Essential for patients with diabetes
Medicines for cholesterol (e.g. statins)	Various minor side effects (e.g. aches and pains)	Part of a wider solution (e.g. diet needed too); Unclear long-term benefits
Vitamin pills	Not risky; Could be issues with over-use	Many people use them unnecessarily; Keeps

		people generally healthy
Blood pressure medicines	Low knowledge of risks; Assume there must be risks	General comments
Flu vaccine	Very mixed responses but generally low risk	Very mixed responses

In describing their perceptions, respondents construed 'risks' in different ways and inconsistently between items. One way that respondents construed 'risks' was as specific side effects with a given treatment. For example, respondents often associated 'medicines to treat depression' with risks of suicide, 'medicines to treat erectile dysfunction' with prolonged erections, and 'X-rays' with risks from repeated use (e.g. cancer) (Table 8). One respondent justified a 3/7 rating for the risks of erectile dysfunction medicines by noting: "*I know that if erections last for more than…four hours is it? That can be a serious problem*". Another gave a 4/7 rating for the risks of medicines to treat depression: "*There are some depression medicines out there that have some risk of suicide especially in adolescents*".

A second way that respondents construed 'risks' was as the dangers of using a treatment inappropriately (Table 8). Sleeping pills were frequently associated with dependency: *"There's a risk of being dependent on them. People may not able to discontinue taking them"* (4/7 risk rating). Insulin was associated with risks of improper administration: *"I would say a four just because some people are not properly using insulin"* (4/7). Several respondents also associated the risks of acupuncture with the skill of the acupuncturist: *"It's like a tattoo artist. The needles could go to the wrong place"* (3/7).

A third way that respondents construed 'risks' was broader than direct side effects and inappropriate use. The risks of antibiotics and prostate screening tests in particular were associated with such risks (Table 8). Antibiotics were often associated with patients *not* being able to have the treatment in the future and *not* being able to benefit from them (i.e.

antimicrobial resistance). These respondents rated the risks of antibiotics as higher than they would otherwise because there was a risk of future patients not being able to use them. One respondent's comments reflected this construal: *"The trouble is that [antibiotics] get over-used"* (4/7 risk rating). In a second example, prostate screening tests were associated with false positives leading to dangerous and unnecessary surgery. One respondent explained why they gave a 5/7 risk rating: *"The risk from [prostate screening tests] is not the test itself but the data they develop leads people to do risky things when they didn't need to. […]. Most men over a certain age have prostate cancer. […]. It leads to unnecessary surgeries because the data leads people to surgeries that don't need"*.

Positive and negative experiences and feelings. The second main way that respondents justified their risk and benefit ratings was to explain their personal positive and negative experiences with different treatments. In so doing, respondents conveyed the 'good' and 'bad' feelings that they associated with different items or what is known as *affect*, defined here as: "the experience (with or without consciousness) of 'goodness' or 'badness' associated with external events and objects or internal representations (e.g. memories)" (p992)[18].[42] The role of affect in respondents' risk and benefit ratings came across most clearly when strong positive and negative personal experiences were associated with a given item.

On the one hand, many respondents provided examples of their positive experiences and hence feelings of 'goodness' associated with a treatment. Such feelings of goodness or positive affect particularly influenced respondents' benefit ratings. One respondent explained how their positive experiences with erectile dysfunction medicines informed their high benefit rating (7/7): **"***Ohhhh. I think those can be very beneficial (laughs). I mean I take them! (laughs). Seven yup I'll go for a seven on that one. Personal experience. They keep us old geezers active"*.

Another respondent explained in detail how their positive experience with heart surgery led to a high benefit rating (6/7): *"Heart surgery has been very beneficial for me. I would give it at least a six. […]. This medicine stuff is a miracle these days. If you think of all of the things that I've been through and I can [still] lead a normal life these days […]".* In a third example, a respondent justified their high benefit rating for blood pressure medicines (6/7): *"They help me. I've had really high blood pressure forever, for 40 years, and [the medicine] doesn't bring it down into the regular range but it brings it down by 50 and it makes a difference".* To be clear, respondents with positive associations to items may have very in-depth knowledge of the treatments from their own personal experience and therefore had 'expert' knowledge. However, what is interesting is the way they justified their answers. They conveyed their own positive experiences and they did not try to identify specific risks and benefits for the broader population.

Respondents positive feelings about different treatments and subsequent ratings were also strongly influenced by family and friends. In many cases, risk and benefit ratings were justified by conveying how their spouses, sibling, parents, friends, and others experienced the treatment. One respondent considered the benefits of statins and gave a high benefit rating based on their husband's experience (6/7): "*I think it's brought my husband's down to an agreeable level".* This shows how again many respondents informed their benefit and risk ratings based on their own experiences and those of family and friends. One respondent attributed their high benefit rating (7/7) for the flu vaccine based on the experiences of their friends: *"Well, I think it's very beneficial. Everybody I know that has ever taken it hasn't gone on to get the flu. The flu can spread easily and for older people it can be really dangerous. […]".* Another respondent gave a similar reason for giving a high benefit rating for their positive feelings about acupuncture (7/7): *"Everyone I've ever heard did well and liked them. It's not painful. It looks like it should*

be but it's not". Respondents' positive experiences with treatments and positive affect therefore had a clear influence on their risk and benefit ratings.

While positive experiences often informed high benefit ratings, many respondents provided examples of their negative experiences with a treatment. In these cases, respondents expressed feelings of 'badness' about different treatments and judged the risks in particular to be high. One respondent explained their strong negative feelings towards cancer chemotherapy which led to a high-risk rating (6/7): *"Oh gosh I'm scared to death of that. I've seen people go through it and they lose their hair, they get dry eyes. They get nausea. You need to be really sick to take those"*. Another respondent explained why they gave X-rays a high-risk rating (5/7): *"I know they were extremely careful with my husband [when he got multiple X-rays for cancer]. There's been a lot in press that you shouldn't do them as many"*. In a third example, a respondent explained why they gave a high-risk rating for the flu vaccine (6/7): *"Because I've seen lots of people having bad reactions. My sister-in-law just got horribly sick from hers. She just had it only a few weeks ago and she had a horrible rash on her arm, and she got very sick. I'm not crazy about the flu shot. I don't want one if I don't have to"*. These negative feelings about different items was perhaps most strongly seen in one respondent's justification for a high rating (6/7) for sleeping pills: "*Because my grandmother died of sleeping pills. It was deliberate but still*". These examples illuminate how personal experiences and negative feelings associated with treatments strongly influenced respondents' risk and benefit ratings.

(4.) Discussion and Conclusion

The overriding goal of this pilot study was to generate experimental evidence that can inform future research comparing patients' pharmaceutical benefit-risk perceptions across the adult

life span. In achieving this goal, the results shed light on major differences and similarities between older and younger adults.

(4.1) General perceptions of prescription medicines

Older versus younger adults were much more likely to associate prescription medicines to images of their benefits such as therapeutic effects and, to a lesser extent, financial expense. Older adults also were more likely to perceive prescription medicines as being effective and self-report experiencing a side effect in the past five years. In contrast, younger adults were much more likely to associate prescription medicines to images of abuse, dependency, and over-prescribing.

One explanation for these age differences may well be that adults aged 58-93 years old use far more prescription medicines than adults aged 31-50.[27,28,43] Kantor *et al*.[43] found that 35% of US adults aged 20-39 years used at least one prescription medicine in 2011-2012 compared to 65% aged 40-64 years and 90% aged 65 years and over. The official statistics body of the EU, Eurostat, reported similar patterns in 2014.[27] In Ireland, 32% of adults aged 35-44 years self-reported prescription medicine use in 2014 compared to 62% aged 55-64 years, 75% aged 65-74 years and 87% aged 75 years and older.[27] Polypharmacy also is much higher in older versus younger populations.[28,43,44] Qato *et al*.[28] found that more than one in three US adults concurrently used five or more prescription medicines in 2010-2011. Greater use may explain why older adults were more likely to associate prescription medicines with their benefits and financial expense, and younger adults to images of dependency, abuse and over-prescribing. While older adults have more to gain therapeutically and bear greater financial costs, younger adults have less to gain therapeutically and bear fewer financial costs. Great use also is accompanied by a high probability of experiencing side effects.

(4.2) Perceptions of past risk

The results show that the majority of both older and younger adults perceive greater risk today than 20 years ago for most items investigated ranging from diabetes and Alzheimer's disease, to adults taking prescription medicines. This is consistent with previous nationally representative research.[1,35,45] Interestingly, older adults were more likely to perceive greater risk today than their younger counterparts for every item except cancer and, to a lesser extent, heart disease. A fruitful area for research would be to verify these (pilot) results and understand why and for which risks older adults are more likely to perceive greater past risk. Such knowledge could help benefit-risk communicators understand how older versus younger adults are more or less sensitive in different hazard contexts.

For prescription medicine risks specifically, both older and younger adults shared similar perceptions of past risk. Almost three quarters of all respondents perceived greater risk from 'adults taking prescription medicines' with little difference between older and younger samples. This result initially appears to conflict with Slovic *et al*.[1] who found that far fewer US adults perceived greater risk today from 'prescription drugs' (-37% difference). This discrepancy, however; may be because the present study specified 'adults taking prescription medicines' whereas Slovic *et al*.[1] specified 'prescription medicines' more generally. This is supported by the finding that 38% of all respondents in the present study perceived more risk today than 20 years ago from 'doctors making prescribing errors'. Respondents therefore were much more likely to perceive greater risk today from adults taking prescription medicines than doctors making prescribing errors (+36%). This emphasises the need for future risk perception studies to pay close attention to the specific referent of judgement when investigating pharmaceutical benefit-risk perceptions.

(4.3) Perceptions of patients and other actors

Other results further support the finding that both older and younger adults have particularly negative perceptions of the role of patients. Few respondents positively rated the ability of patients to take medicines safely and effectively. Rather, the patient's role in taking prescription medicines was rated much more negatively than all other actors including regulatory agencies, pharmaceutical companies, prescribing doctors, and especially pharmacists. The majority of respondents also perceived 'patients not following medication instructions' and 'patients receiving insufficient information' as two of the most frequent causes of side effects. This general pattern supports past research with Slovic *et al*.[1] finding the same ordering and similar values. Other nationally representative studies also consistently show that adults in the United States and Europe are more likely to trust their pharmacist than almost any other actor and view them as a key source of benefit-risk information.[46-47]

Curiously, older versus younger adults were much more likely to rate prescribing doctors as excellent or good (+35% difference). The authors are unaware of any studies identifying substantial differences between how older and younger adults perceive the ability of their doctors. On the one hand, this finding may be an erroneous outlier. The study had a convenience sample and there is no clear evidence of nationally representative research identifying such an age-related difference. On the other hand, few studies have reported age-related results on how older versus younger respondents perceive the ability of prescribing doctors. Understanding whether these results are spurious or accurate could be tested in nationally representative surveys. If a significant difference between older versus younger perceptions of prescribing doctors is supported, there will be important implications for benefit-risk communication.

(4.3) Justifying Benefit-Risk Ratings

When analysing older and younger respondents' benefit-risk ratings, a familiar pattern was found. Most medicines, medical procedures and tests were rated as high-benefit and low-risk. Some items – vitamin pills, Alzheimer's medicines, herbal medicines, acupuncture – were perceived as lower in benefit than the majority of pharmaceutical items. A few other items – cancer chemotherapy, heart surgery, sleeping pills, depression medicines – were rated as higher-risk that all other medical items. In contrast, most non-medical items ranging from cigarette smoking to nuclear power plants and genetically modified food, were perceived as low-benefit and high-risk. This pattern and clustering of medical and non-medical items is highly consistent with past studies including those conducted with nationally representative samples.[1,21,48] They also support recent findings that patterns of public risk perceptions remain "practically unchanged" since they were first investigated in the late 1970s, albeit with a few notable exceptions.[49]

Interestingly, older respondents were more likely than their younger counterparts to perceive lower risk for over three quarters of medical and non-medical items surveyed. While little research has been conducted in the pharmaceutical domain, past studies conducted in other contexts support these results by showing that older versus younger adults perceive lower risk for a wide variety hazards.[20,50,51] Greenberg[20], for example, surveyed the environmental risk perceptions of US adults aged 75 years old and over. Older versus younger adults were less concerned about almost every environmental risk examined including water quality, open space, traffic congestion and other chronic issues.[20] In contrast, older adults' risk perceptions were much closer to those of their younger counterparts for acute risk issues such as nuclear facility failures and natural hazard events.[20] However, other studies have found the opposite

effect with older versus younger adults perceiving greater risk.[52-54] Siegrist *et al*.[54], for example, found that older versus younger adults perceived significantly greater risk for various technological, social and natural hazards. The wide variation in empirical findings examining whether older versus younger adults perceive greater risk or not suggests that a more sophisticated approach is needed. In particular, understanding which age groups perceive more or less risk *in general* may be a Sisyphean task. A more fruitful line of inquiry, as this study suggests, would be to understand under which conditions, and for which hazards, older versus younger adults perceive more or less risk.

Beyond comparing benefit-risk perceptions, a key aim of this study was to explore, qualitatively, how older adults justified their quantitative benefit-risk ratings (section 3.7). When justifying their ratings, older adults construed 'risk' in at least three main ways: (1) as side effects, (2) as dangers of improper use, and (3) as wider issues. This variation strongly questions whether general measures of benefit-risk perceptions can be used in future studies to identify age-related differences. For example, one respondent rated the risks of sleeping pills by considering the risks of dependency (improper use). To what extent can this respondent's rating be compared with that of another who, quite reasonably, only considered side effects such as 'patients being drowsy the following morning'? Would the second respondent have changed their rating if they believed that improper use was an acceptable consideration in their quantitative risk judgement? The results therefore show that future study designs, and especially those examining age-related differences, need to distinguish clearly between different construes of risk (and benefit).

A second key finding was that older adults' personal experiences had a strong influence on their pharmaceutical benefit-risk perceptions. Treatments that were associated with

positive/negative experiences and feelings of 'goodness'/'badness' strongly influenced respondents' benefit-risk ratings. While positive experiences/affect were associated with high benefit ratings, negative experiences/affect were associated with high risk ratings. A major body of risk perception research has emphasised the importance of affect (and emotion) on perceptions of risk (and benefit).[42,55,56] To be clear, this is not to say that emotion and affect determine older adults' benefit-risk decisions. Rather, older adults' judgements and decisions were influenced by the negative/positive feelings they associated with different treatments. This is an important distinction as, in real-world contexts, prescription medicine decisions are not made in a vacuum. As McNutt[31] explains: "Physicians should ensure that the information used in the patient's decision making is reasonable for the individual patient and that the patient understands the ramifications of choice. The physician should be a navigator, not a pilot".

The strong influence of 'risk as feelings' provide support for Slovic *et al*.'s[1] suggestion that a high negative correlation between pharmaceutical benefit and risk is due to a "reliance on the affect heuristic". Moreover, the present study provides a rich understanding and description of the influence of affect for various medical treatments. Older adults also were clearly influenced by their personal experiences and those of close family and friends. However, the study did not provide evidence as to whether older adults were more likely to rely on affective processes than their younger counterparts or not. This presents an important line of inquiry for future research. In particular, psychological judgement and decision-making studies, conducted primarily in nonpharmaceutical contexts, have consistently found that older versus younger adults rely more heavily on affective processes.[17,18,56] The results of this study provide strong evidence that understanding age-related differences in affective processes would be a fruitful area for future research.

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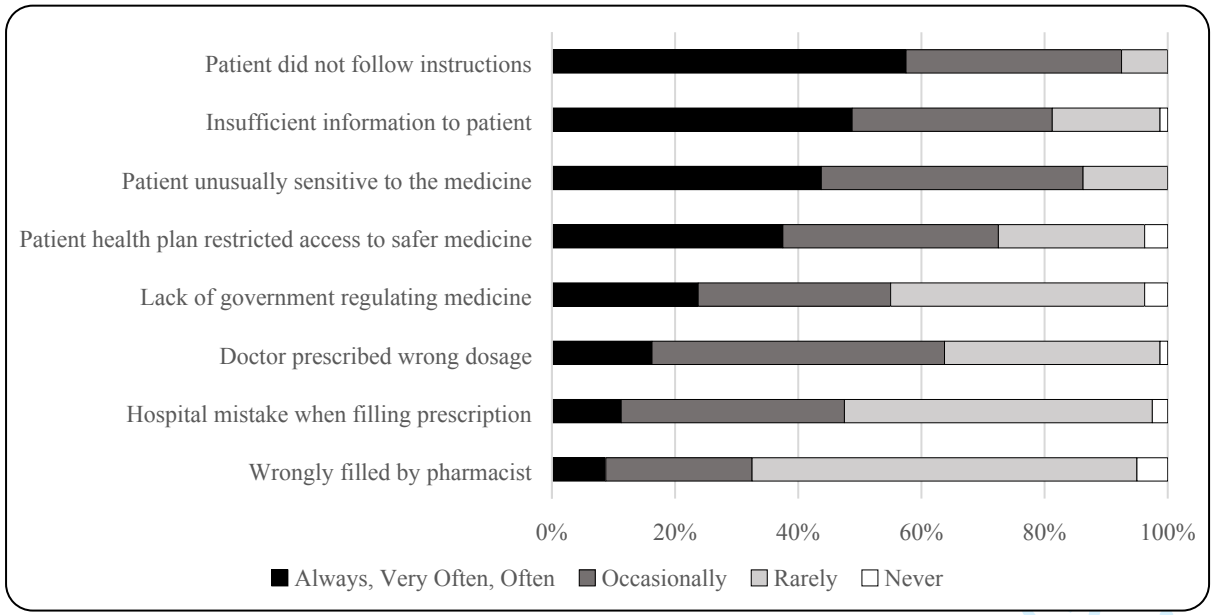

Figure 1: Bar chart showing how often all respondents (N=80) think side effects are caused by various explanations.

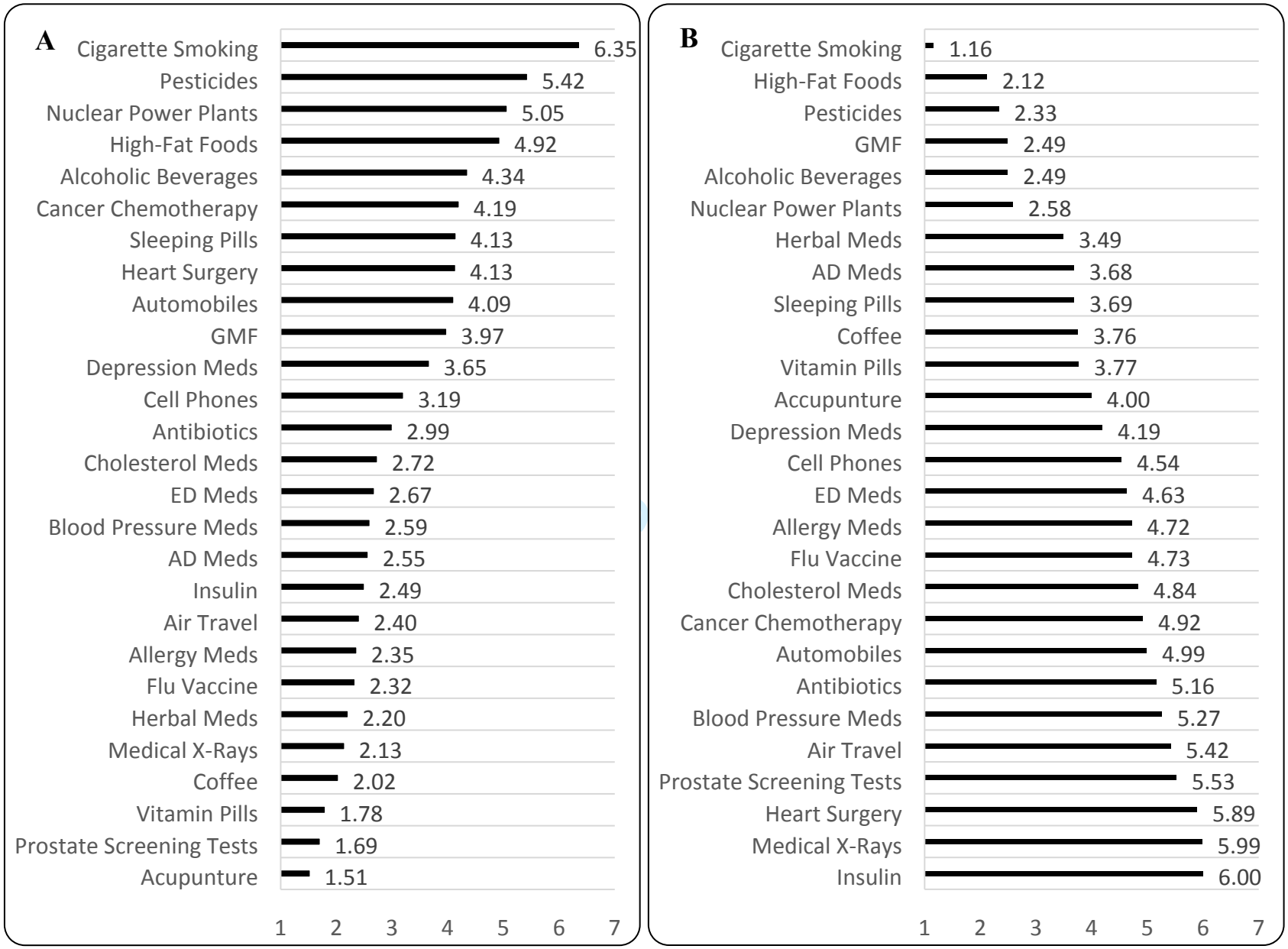

Figure 2:
(A) Mean Risk
(B) Mean Benefit
GMF: Genetically Modified Food
ED: Erectile Dysfunction
AD: Alzheimer's Disease

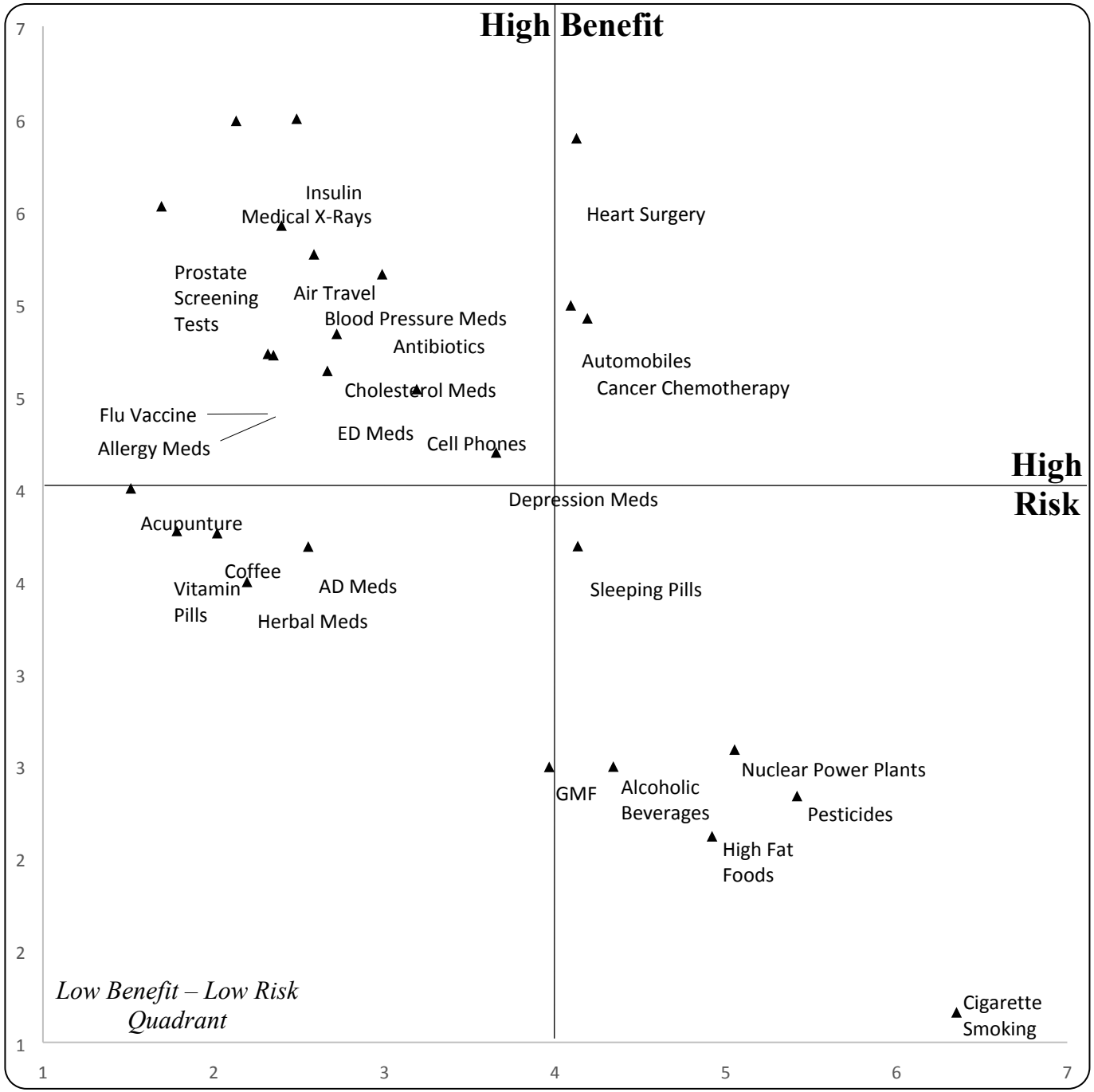

Figure 3: Plot of Benefit and Risk Means.
GMF: Genetically Modified Food
ED: Erectile Dysfunction
AD: Alzheimer's Disease

Table 1: Demographic and health information for older and younger samples

		Older Sample	Younger Sample
Dates		Nov. 1st – 10th, 2017	Feb 1st – 14th, 2018
Sample size		40	40
Age Range		58 to 93	31 to 50
Mean Age		72	39
Male		44%	45%
Education (%)	*Some schooling complete/ No high school diploma*	23%	0%
	High School Graduate or Equivalent	18%	30%
	Bachelor's Degree	21%	50%
	Master's Degree	36%	20%
	Professional/ Doctorate Degree	3%	0%
Employment (%)	*Working Full-Time*	13%	45%
	Working Part-Time	23%	25%
	Retired	64%	3%
	Full Time Homemaker	0%	5%
	Unemployed (looking for work)	0%	8%
	Student	0%	10%
	Other	0%	5%
Do you currently have a doctor? (%)	*Yes*	97%	60%
Do you currently smoke? (%)	*Yes*	0%	35%

Table 2: Sixteen hazard items

Air travel	Heart disease
Adults getting Alzheimer's disease	Hurricanes
Cancer	Adults getting HIV/AIDS
Climate change	Nuclear power
Diabetes	Pesticides
Driving a car	Adults taking prescription medicines
Doctors making prescribing errors	Train travel
Flooding	Chemicals

Box 1: Psychometric risk and benefit questions

Risks of medical technologies (to those exposed). To what extent would you say that adults who are taking or undergoing this medical treatment are at risk[1] of experiencing personal harm from it? (1 = they are not at risk; 7 = they are very much at risk)
Benefits of medical technologies. In general, how beneficial do you consider this treatment to be? (1 = not at all beneficial; 7 = very beneficial)
Risks of non-medical technologies (to those exposed). To what extent would you say that adults who are exposed to the following are at risk[2] of experiencing personal harm from it? (1 = they are not at risk; 7 = they are very much at risk)
Benefits of non-medical technologies. In general, how beneficial do you consider the following items to be for those exposed to it? (1 = not at all beneficial; 7 = very beneficial)

Table 3: Medical and non-medical items surveyed

Medicines	Medical Procedures & Tests	Non-Medical Technologies

[1] 'Risk' was intentionally not defined. Respondents were left to interpret what 'risk' meant for each technology.

Medicine to treat depression	Heart surgery	Cell phones
Medicines to slow the progression of Alzheimer's disease	Medical x-rays	Nuclear power plants
Medicines to treat erectile dysfunction	Prostate screening tests	Pesticides
Antibiotics	Acupuncture	Cigarette smoking
Sleeping pills		High-fat foods
Herbal medicines		Genetically modified food
Cancer chemotherapy		Automobiles
Insulin		Alcoholic beverages
Medicines for cholesterol (e.g. statins)		Coffee
Vitamin pills		Air travel
Blood pressure medicines		
MMR vaccine		
Flu vaccine		
Allergy medicines		

Table 4: Spontaneous imagery associated to "Prescription Medicines"

	Older (%)	**Younger (%)**	**All (%)**
Helpful/Beneficial/Good	24	7	11
HCPs (e.g. "My Doctor")	14	16	15
Types of Disease and Illness	12	11	11
Expensive	10	2	6
Names of Specific Drugs	9	9	9
Side Effects	8	7	7
Own and Family Prescription Medicines	6	3	5
Dependency/Abuse/Over-Prescribing	5	15	10
Annoying/Want to Avoid if Possible	4	5	5
Industry Profits	2	4	3
General Safety	1	5	3
Other (e.g. Packaging)	7	15	14
No. of Responses	**93 (count)**	**94 (count)**	**187 (count)**

Table 5: Percentage of all respondents (N=80) for the question: 'Do you think there is more, less, or about the same risk today than 20 years ago for the following items?'

	More	**Less**	**About the Same**
Climate Change	94	3	4
Diabetes	78	11	11
Flooding	76	6	18
Adults Taking Prescription Medicines	74	13	14
Hurricanes	71	4	25
Cancer	69	11	19
Chemicals	69	16	15
Adults Getting Alzheimer's Disease	65	8	26
Heart Disease	65	11	24
Pesticides	63	24	14
Driving a Car	53	29	19
Nuclear Power	50	23	28
Doctors Making Prescription Errors	48	21	30
Adults Getting HIV	35	53	10
Air Travel	34	50	16
Train Travel	19	46	35

Table 6: Table showing the percentage (%) of older and younger group respondents that rated five actors as either excellent or good in making sure that prescription medicines are safe and effective.

	Older (%)	Younger (%)	All (%)
Pharmacists	80	70	75
Prescribing Doctors	73	38	55
Pharma Companies	50	40	45
Regulatory Agencies	48	38	43
Patients	33	23	28

Table 7: Respondents perceptions of effectiveness and side effects. Effectiveness: "How often do you believe that prescription medicines work as intended for patients?" Side Effects: "How often do you believe that patients experience unwanted effects or side effects from prescription medicines?"

	Effectiveness			**Side Effects**		
	Older (%)	Younger (%)	All (%)	Older (%)	Younger (%)	All (%)
Always	0	3	1	3	10	6
Very Often	43	20	31	20	18	19
Often	58	55	56	43	30	36
Occasionally	0	23	11	30	33	31
Rarely or Never	0	0	0	5	10	8

Table 8: Older respondents' (N=40) most common risk and benefit associations for all pharmaceutical items.

Item	**Risks**	**Benefits**
Medicines to treat depression	Suicide; over-dose; incorrect use	Benefits vary between patients; Patients need appropriate medicines
Medicines to treat Alzheimer's Disease	Low knowledge of any risks	Low knowledge of any benefits
Medicines to treat erectile dysfunction	Most unaware of any risks; Prolonged erections	Very effective for those who need them
Antibiotics	Antimicrobial resistance and over-use	Antimicrobial resistance reduces benefits
Sleeping pills	Over-dose; Dependency	Can really help patients fall asleep
Herbal medicines	Not harmful; Lack of regulation	Unconvinced about any benefits; False claims
Cancer chemotherapy	Risky treatment; Only hope for some people	Lifesaving for some; Many regret chemotherapy
Insulin	Few risks except with inappropriate use	Essential for patients with diabetes
Medicines for cholesterol (e.g. statins)	Various minor side effects (e.g. aches and pains)	Part of a wider solution (e.g. diet needed too); Unclear long-term benefits
Vitamin pills	Not risky; Could be issues with over-use	Many people use them unnecessarily; Keeps people generally healthy
Blood pressure medicines	Low knowledge of risks; Assume there must be risks	General comments
Flu vaccine	Very mixed responses but generally low risk	Very mixed responses

Allergy medicines	No clear risks except over-doses	Helpful for people with allergies
Heart surgery	Any surgery comes with risk; Heart surgery has a serious risk of death	Heart surgery is essential if you need it
X-rays	Risks from repeated use (e.g. cancer)	A necessity
Prostate screening tests	Little risk from the actual test; Serious side effects with false positive	Beneficial and lifesaving when tests are accurate
Acupuncture	Generally harmless; Requires a safe acupuncturist	Can reduce pain but unclear why; Worth trying